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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------------------|-----------------------------|
| 10/597,357 | 07/21/2006 | Hiroaki Shimokawa | P30188 | 9832 |
| 7055 7590 09/10/2009 GREENBLUM & BERNSTEIN, P.L.C. 1950 ROLAND CLARKE PLACE RESTON, VA 20191 | | | EXAMINER FINN, MEGHAN R | |
| | | | ART UNIT 1614 | PAPER NUMBER |
| | | | NOTIFICATION DATE 09/10/2009 | DELIVERY MODE ELECTRONIC |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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| | | | |
|------------------------------|-------------------------------|------------------------------------|--|
| Office Action Summary | Application No. 10/597,357 | Applicant(s) SHIMOKAWA, HIROAKI | |
| | Examiner MEGHAN FINN | Art Unit 1614 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 May 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) 1-4 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 5-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>7/09/09; 5/01/09; 9/1/09</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's Amendment filed May 01, 2009 has been received and entered into present application. No claims were canceled and claims 9-12 were added by applicant. Claims 1-4 remain withdrawn and thus claims 5-12 are under examination.

Applicants' arguments, filed May 01, 2009, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Applicant submitted identical Information Disclosure Statements (IDS) on May 01, 2009 and July 09, 2009. Only the abstract of the Hui-yu et al., reference was in English and thus that was all that was considered on the May 01, 2009 IDS. Since the July 09, 2009 IDS was a duplicate none of those references were marked considered to avoid duplication. In the IDS submitted September 01, 2009 the Batchelor et al. reference is already of record and therefore not considered to avoid duplication.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 5-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Batchelor et al. (Rho-kinase inhibitors prevent agonist-induced vasospasm in human internal mammary artery, already of record in the previous office action mailed February 05, 2009) in view of Trimboli et al. (Coronary artery spasm after off-pump coronary artery bypass grafting).

Applicant has amended the claims such that they now read upon a method of treating vasospasms caused by an off pump beating coronary artery bypass grafting with a compound of formula I, which encompasses fasudil or hydroxyfasudil. As discussed in the previous office action, fasudil is also known as HA1077 and Batchelor et al. teaches that vasospasms are an important problem in the recovery from bypass graft surgery and the causes are multi-factorial (page 302, paragraphs 1-2). They also teach that HA1077 was a relaxant (point 3 of abstract) and that Rho-kinase-inhibitors (such as HA1077) play an important role in preventing vasospasms (point 5 of abstract). They further teach that common L-type Ca^{2+} channel blockers such as verapamil as well as nitrates often are ineffective against such vasospasm (page 302, 3rd paragraph). Additionally, they teach that HA1077 completely reversed the submaximal contraction caused by administration of U46619 (which was used to cause contraction as demonstrated in figure 1, page 304). Thus it would have been obvious to one of ordinary skill in the art at the time of the invention that HA1077 can be used to treat vasospasms, including those that do not respond to drugs such as verapamil or nitrates. Batchelor et al. does not teach treating patients that have undergone off pump beating

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coronary artery bypass grafting, however Trimboli et al. teaches that coronary artery spasms are a problem in off pump coronary artery bypass (OPCAB) and describe a patient who experienced persistent coronary spasms after surgery (page 830, background). They further teach that coronary artery spasms reportedly occur in up to 1.3% of patients and it is suspected that even higher percentage is present that are undiagnosed (pave 832, paragraph 5). It would have been obvious to one of ordinary skill in the art at the time of the invention that fasudil (HA1077) can be used to treat and reduce the number of vasospasms occurring after surgery, and given then that coronary artery spasms, which are a type of vasospasm, are a problem in off pump beating coronary artery bypass grafting it would be obvious to use a known treatment for vasospasms on those patients. Even more motivation to use fasudil on patients that did not respond to the calcium antagonists and nitrate compounds that are reportedly ineffective in some patients (Batchelor, page 302). In claims 6-12, applicant claims specific locations for the vasospasms and grafting location, however one of ordinary skill in the art at the time of the invention would have no reason to believe that fasudil would not treat the vasospasm regardless of location. Thus claims 5-12 are unpatentable over Batchelor et al. in view of Trimboli et al.

Conclusion

No Claims of the present application are allowed.

New rejections of claims 5-12 are necessitated by the amendment to the claims.

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Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Meghan Finn whose telephone number is (571) 270-3281. The examiner can normally be reached on 8:30am-6pm Mon-Thu, 8:30am-5pm Friday (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Meghan Finn

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614